REMARKS

The Summary of the Invention, paragraph 32, and claims 1, 2, 14, and 26 of the captioned application were amended to remove the previously added quotient of the ratio of simethicone to adsorbent. Support for this amendment can be found throughout the specification at, for example, the original Summary of the Invention, paragraph 32, and claims 1, 2, 14, and 26.

Paragraph 9 was amended to correct factual misstatements in the last sentence. Support for the amendments to paragraph 9 can be found in US Pat. No. 6,103,260 at col. 4, lns. 45-50.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

The undersigned wishes to thank the Examiner for the courtesies extended during the August 6, 2003 Interview with the undersigned and inventor Szymczak. Paper No. 10 reflects the substance of the Interview.

Restriction Requirement

The Examiner maintained the provisional election of famotidine as the elected species. (Paper No. at 2-3.) Claims 6 and 18 have been withdrawn as being directed to a non-elected invention. (Id. at 3.) Upon allowance of a generic claim or the elected species, the Examiner is asked to consider the claims to the elected species which are written in dependent form or otherwise include all the limitations of an allowed generic claim.

New Matter Objection

The Examiner objected to the explicit disclosure of the quotient obtained by the ratio of simethicone to adsorbent. (Paper No. 9 at 3.) In particular, the Examiner contended that the quotients were "not supported by the original disclosure." The Examiner reasoned that the term "'at least about 1:2.22' relates to the range of weight ratio of simethicone to adsorbent, for example 1:2.20, 1:2.21, 1:2.22, 1:2.23, 1: 2.24, 1:2.25, 1:2.26, 1:2.27, 1:2.28, etc." (*Id.* at 4.) The Examiner further reasoned that a ratio of 1:1.111 "does not fall within "at least 1:2.22", nor "at least about 1:1.80, nor "at least 1 part simethicone to 1.75 parts adsorbent." (*Id.*) The Examiner applied similar reasoning

to "at least about 0.5", "at least about 0.56", and "at least about 0.57." (*Id.*) The Examiner then required cancellation of the alleged new matter. (*Id.*)

The contentions and reasoning employed by the Examiner in Paper No. 9 rests on the presumption that the Examiner's interpretation of the ratios of simethicone to adsorbent is correct. For, if they are not correct, the entire basis for the objection and rejections become highly suspect. In fact, if one were to apply the Examiner's reasoning to interpret claim 2 in light of claim 1 as required by 35 USC § 112, fourth paragraph, one would be at a disadvantage because one could not properly interpret claim 2 using the reasoning employed by the Examiner. However, it appears that the Examiner failed to properly interpret claim 2 and relied on the reasoning set forth for claim 1 for all the claims.

The Examiner is asked to consider the following: interpreting claim 2, which requires among other things, a ratio of simethicone to adsorbent of at least 1:2.00 together with all the limitations of claim 1, including among other things, a ratio of simethicone to adsorbent of at least 1:2.22, requires the exact opposite reasoning set forth by the Examiner to not run afoul of 35 USC § 112, second paragraph. In fact, claim 2 actually requires more simethicone per adsorbent than claim 1. It is respectfully submitted that the example postulated by the Examiner, 1:1.11, falls squarely within the scope of the claims – all of the claims. For this reason, the objection is improper and should be withdrawn.

While not agreed with for the reasons set forth above, the quotients added in the January 31, 2003 Response have been cancelled by amendment to the specification and the claims. Because the quotients have been removed, it is submitted that this objection is moot and should be withdrawn.

Written Description Rejection

Claims 1-5, 7-12, 14, and 26 were rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. (Paper No. 9 at 5.) The Examiner contended that "the claim(s) contain subject matter that was not described in the specification in such a way to convey that to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

(*Id.*) In making the rejection, the Examiner asserted that "[the reasoning of this rejection has been discussed in above new matter objection under 35 USC § 132." (*Id.*)

As set forth above, while not agreed with, the quotients added in the January 31, 2003 Response have been cancelled by amendment to the specification and the claims. Because the quotients have been removed, it is submitted that this rejection is moot and should be withdrawn.

Anticipation Rejection

Claims 1-2 and 4-5 were rejected under 35 USC §102(b) as anticipated by Stevens, US Patent No. 5,679,376, ("Stevens"). (OA at 5.)

For the reasons set forth below, the rejection, respectfully is traversed.

Stevens' disclosure set forth in the January 31, 2003 Response filed by the undersigned in the captioned application is incorporated herein by reference.

In making the rejection, the Examiner merely stated that "[t]his rejection is analogous to the original rejection." (Paper No. 9 at 5.) In the original rejection, the Examiner contended only that "Stevens teaches a solid oral dosage form comprising loperamide, simethicone, microcrystalline cellulose and colloidal silicone dioxide, wherein a ratio of simethicone and microcrystalline cellulose is about 1.2.12 (125 mg :265.5 mg) or a ratio of simethicone and a combination of colloidal silicon dioxide and microcrystalline cellulose is about 1:2.37 (125 mg:297 mg). (Paper No. 5 at 5.) The Examiner appears to have taken official notice that the use of microcrystalline cellulose and colloidal silicon dioxide were inherently adsorbents. Further, the Examiner concluded that since the calculated ratio of 1:2.12 (simethicone to microcrystalline cellulose) or 1 2.37 (simethicone to the combination of microcrystalline cellulose and colloidal silicon dioxide) fell within the claimed ration of simethicone to adsorbent of at least about 1:2.22 (claim 1) and at least 1:2. (*Id.*)

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim.

We note that the Examiner asserted that dibasic calcium phosphate "falls within the broadly defined adsorbent." (Paper No. 5 at 6-7.) The example relied upon by the Examiner in the instant rejection discloses using 370 mg of dibasic calcium phosphate,

USP. It appears that the Examiner may have overlooked this fact in making the instant rejection.

The claimed ratios of simethicone to adsorbent were converted to their quotients in an attempt to aid the Examiner in understanding the instant invention. Using this ratio, it is clear that Stevens does not disclose as much as the Examiner asserted. For example, the sole example in Stevens relied on by the Examiner provides factual evidence that the ratio of simethicone to adsorbent (dibasic calcium phosphate + microcrystalline cellulose + colloidal silicon dioxide) is 125:667, or 1:5.34. It is submitted that a ratio of 1:5.34 does not fall within the scope of the claimed subject matter as properly interpreted. For this reason, the rejection is improper and should be withdrawn.

Because claims 2, 4, and 5 depend from claim 1, the rejection to these claims based on Stevens is also improper and should be withdrawn.

Claims 1-2, 4-5. 7-8, and 11-12 were rejected under 35 USC §102(b) as anticipated by Luber et al., US Patent No. 6,103,260, ("Luber"). (Paper No. 9 at 5.)

For the reasons set forth below, the rejection respectfully is traversed.

Luber's disclosure set forth in the January 31, 2003 Response filed by the undersigned in the captioned application is incorporated herein by reference.

In making the rejection, the Examiner merely stated that "[t]his rejection is analogous to the original rejection." (Paper No. 9 at 5.) In the original rejection of claims 1-2, the Examiner asserted that "Luber teaches an antifoam oral solid dosage form preparations formed from a free [f]lowing granular composition comprising an admixture of simethicone and [] either one or both of granular anhydrous tribasic calcium phosphate or dibasic calcium phosphate, wherein the simethicone is adsorbed by the granular anhydrous tribasic or dibasic calcium phosphate or mixture thereof, and where ratios of simethicone to granular tricalcium phosphate are 1:3.5 in Examples 1-2 and 1:4 in Example 6. (OA at 6.) The Examiner further asserted "[a]lthough Luber is silent about the use of granular tribasic calcium phosphate or dibasic calcium phosphate as an adsorbent" such compounds "read[] on the broadly defined term "adsorbent." Based upon this, the Examiner concluded that "the reference clearly anticipates the claimed invention" because "the claimed weight ratio of simethicone to adsorbent" encompasses

the weight ratio of simethicone to tribasic calcium phosphate or dibasic calcium phosphate disclosed in Luber.

As is well settled, anticipation requires "identity of invention." Each and every element recited in a claim must be found in a single prior art reference and arranged as in the claim.

The claimed ratios of simethicone to adsorbent were converted to their quotients in an attempt to aid the Examiner in understanding the instant invention. Using this ratio, it is clear that Luber does not disclose as much as the Examiner asserted. For example, the Examiner asserted that the ratios of simethicone to granular tricalcium phosphate were 1:3.5 in Examples 1-2 and 1:4 in Example 6. It is submitted that a ratio of about 1:3.5 and 1:4 do not fall within the scope of the claimed subject matter as properly interpreted. For this reason, the rejection is improper and should be withdrawn.

Because claims 2, 4-5. 7-8, and 11-12 depend from claim 1 under the doctrine of claim differentiation, the rejection to these claims based on Luber is also improper and should be withdrawn.

Obviousness Rejection

Claims 3, 9-10, 13-15, and 19-26 were rejected under 35 USC §103(a) as being unpatentable over Kitsusho Yakuhin Kogyo KK (JP 398241) ("Kitsusho") in view of Tobyn et al, (International Journal of Pharmaceutics 169 (1998) 183-194) ("Tobyn") (OA at 9.)

For the reasons set forth below the rejection, respectfully is traversed.

Kitsusho's disclosure set forth in the January 31, 2003 Response filed by the undersigned in the captioned application is incorporated herein by reference.

Tobyn's disclosure set forth in the January 31, 2003 Response filed by the undersigned in the captioned application is incorporated herein by reference. In addition, at page 191, Tobyn discloses that, among other things, "[t]he values obtained relating to the total pore areas, the median pore diameters and the porosities of the samples ... pore sizes were found to be very similar ... it is interesting to that there is no apparent increase in accessible surface area with the SMCC90 sample, whereas there is with dry mixes of silicon dioxide and MCC."

In making the rejection, the Examiner merely stated that "[t]his rejection is analogous to the original rejection." (Paper No. 9 at 6.) In the original rejection, the Examiner asserted that Kitsusho teaches "teaches a method for preparing simethicone tablets by mixing and granulating simethicone with magnesium aluminum metasilicate. (OA at 9.) The Examiner further asserted that the "formulation disclosed by Kitsusho requires at most 25% simethicone and 75% or greater silicate, binder (i.e., starch and lactose) and dispersing agents (i.e., carboxymethylcellulose)." (OA at 9-10.) The Examiner also contended that " [Kitsusho] teaches that when the amount of simethicone exceeds 25% there is a tendency that a portion of the simethicone can be carried away, therefore the tablet workability is not desirable." (OA at 10.) The Examiner acknowledged, however, that Kitsusho differs from the presently claimed invention in that:

1. the incorporation of silicified microcrystalline cellulose in said composition;
2. at least 30 wt% simethicone in said composition;
3. the specific amounts of silicified microcrystalline cellulose and magnesium aluminometasilicates in said composition; and
4. the specific har[d]ness of value of the tablet. (OA at 10.)

To fill the acknowledged gap, the Examiner relied upon Tobyn as disclosing the advantage of using silicified microcrystalline cellulose in improving tablet workability such as "powder flow," "tablet strength," "lubricant sensitivity" and "wet granulation." (*Id.* at 10.)

The Examiner then concluded that "[t]o incorporate such teaching into the teaching of Kitsusho, would have been obvious in view of Tobyn, who teaches the advantage of using silicified microcrystalline cellulose as a pharmaceutical excipient [] to improve powder flow characteristics, lubricant sensitivity, tablet strength and better bulk physical properties. (*Id*). The Examiner reasoned that that "[o]ne having ordinary skill in the art would have been motivated, with a reasonable expectation of success, to incorporate silicified microcrystalline cellulose having good free-flowing and disintegrating properties (which is relatively new pharmaceutical excipients in the art) such that the table workability would be significantly improved. (*Id.*) The Examiner

reasoned further "one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition." (OA at 10-11.)

The Examiner then asserted that "[a]lthough the prior art references are silent about the specific dosage amounts of active ingredients and the hardness value of tablet, the optimization of [known] active and inactive ingredients in a composition or the determination of optimum hardness value of the tablet is well considered within the skill of the artisan, absent evidence to the contrary."

Obviousness, cannot be based upon speculation. Nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." When a conclusion of obviousness is not based upon facts, it cannot stand.

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

The rejection uses Tobyn to fill in the acknowledged gaps in Kitsusho, but it does not appear that the Examiner considered all of Tobyn's disclosure in making the rejection. For example, Tobyn discloses that, among other things,

> "[t]he values obtained relating to the total pore areas, the median pore diameters and the porosities of the samples ... pore sizes were found to be very similar ... it is interesting to that there is no apparent increase in accessible surface area with the SMCC90 sample, whereas there is with dry mixes of silicon dioxide and MCC." (Tobyn at 191.)

It is not seen where the record provides any motivation or suggestion to use SMCC90 over MCC to increase loading, especially where there was no increase in accessible surface area. Because the record provides no expectation of success, the rejection is improper and should be withdrawn.

In addition, the rejection also fails to point out where in Tobyn even one experiment using simethicone is disclosed. The rejection then summarily concludes that one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition.

However, the rejection does not support such a conclusion. It is not seen where in the rejection the Examiner provided any facts in Tobyn to indicate that simethicone, a viscous oil-like substance, could be adsorbed onto silicified microcrystalline cellulose, much less any facts indicating that silicified microcrystalline cellulose would have the same improved properties when formulated with simethicone. Thus, for this additional reason, the rejection is not supported by fact and must be withdrawn for this reason alone.

Further, the Examiner has not provided any facts to support the proposition that using siMCC in Kitsusho's formulation would overcome the problem acknowledged by Kitsusho, e.g., not exceeding 25% simethicone in the formulation. It is not seen where there are any facts in the rejection to suggest any expectation of success for increasing the amount of simethicone in a formulation using an additional adsorbent, e.g., siMCC. Because it appears that the rejection is based upon possibilities or probabilities, it is improper and should be withdrawn.

Claims 16 and 17 were rejected under 35 USC §103(a) as being unpatentable over Kitsusho in view of Tobyn and Stevens. (OA at 11.)

For the reasons set forth below the rejection, respectfully is traversed.

The disclosures of Kitsusho, Tobyn, and Stevens set forth above are herein incorporated by reference.

In making the rejection, the Examiner merely stated that "[t]his rejection is analogous to the original rejection." (Paper No. 9 at 6.) In the original rejection, the Examiner asserted that "the modified teach of Kitsusho includes all that is recited in claims 16 and 17 except for the incorporation of active pharmaceuticals such as

famotidine. (OA at 11.) To fill the acknowledged gap, the Examiner relied on Stevens as "teach[ing] or suggest[ing] the use of simethicone and other pharmaceutical excipients in preparing oral solid dosage form containing H2 blockers (e.g.., famotidine). (OA at 11.)

The Examiner contended that "[o]ne having ordinary skill in the art would have know that simethicone is routinely combined with H2 blockers such as famotidine in solid oral dosage formulation art, and would have been further motivated to further modify the teaching of Kitshusho such that the better solid dosage form containing famotidine would be formulated. (OA at 11.) The Examiner reasoned "[o]ne having ordinary skill in the art would have been motivated to do this so that the tablet workability would be significantly improved." (OA at 11.)

Obviousness, cannot be based upon speculation. Nor can obviousness be based upon possibilities or probabilities. Obviousness ***must*** be based upon facts, "cold hard facts." When a conclusion of obviousness is not based upon facts, it cannot stand.

"Determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 546, 48 USPQ2d 1321, 1329 (Fed. Cir. 1998). There must be a teaching or suggestion within the prior art, within the nature of the problem to be solved, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources, to select particular elements, and to combine them as combined by the inventor. See Ruiz v. A.B. Chance Co., 234 F.3d 654, 665, 57 USPQ2d 1161, 1167 (Fed. Cir. 2000); ATD Corp, 159 F.3d at 546, 48 USPQ2d at 1329; Heidelberger Druckmaschinen AG v. Hantscho Commercial Prods., Inc., 21 F.3d 1068, 1072, 30 USPQ2d 1377, 1379 (Fed. Cir. 1994) ("When the patented invention is made by combining known components to achieve a new system, the prior art must provide a suggestion or motivation to make such a combination.").

The rejection uses, among other things, Tobyn to fill in the acknowledged gaps in Kitsusho, but it does not appear that the Examiner considered all of Tobyn's disclosure in making the rejection. For example, Tobyn discloses that, among other things,

> "[t]he values obtained relating to the total pore areas, the median pore diameters and the porosities of the samples ... pore sizes were found to be very similar ... it is interesting to that there is no apparent increase in accessible surface

> area with the SMCC90 sample, whereas there is with dry mixes of silicon dioxide and MCC." (Tobyn at 191.)

It is not seen where the record provides any motivation or suggestion to use SMCC90 over MCC to increase loading, especially where there was no increase in accessible surface area. It is not seen where Stevens addresses the lack of any expectation of success created by Tobyn. Because the record provides no expectation of success, the rejection is improper and should be withdrawn.

In addition, the rejection also fails to point out where in Tobyn even one experiment using simethicone is disclosed. The rejection then summarily concludes that one having ordinary skill in the art would have been motivated to increase the amount of simethicone above 25% in the solid final blend for tableting by incorporating silicified microcrystalline cellulose in said composition.

However, the rejection does not support such a conclusion. It is not seen where in the rejection the Examiner provided any facts in Tobyn to indicate that simethicone, a viscous oil-like substance, could be adsorbed onto silicified microcrystalline cellulose, much less any facts indicating that silicified microcrystalline cellulose would have the same improved properties when formulated with simethicone. Thus, the rejection is not supported by fact and must be withdrawn for this reason alone.

Further, the Examiner has not provided any facts to support the proposition that using siMCC in Kitsusho's formulation would overcome the problem acknowledged by Kitsusho, e.g., not exceeding 25% simethicone in the formulation. It is not seen where there are any facts in the rejection to suggest any expectation of success for increasing the amount of simethicone in a formulation using an additional adsorbent, e.g., siMCC. Because it appears that the rejection is based upon possibilities or probabilities, it is improper and should be withdrawn.

Finally, Stevens does appear to close the gaps in the Examiner's rejection. The sole example in Stevens relied on by the Examiner provides factual evidence that the ratio of simethicone to adsorbent (dibasic calcium phosphate + microcrystalline cellulose + colloidal silicon dioxide) is 125:667, or 1:5.34. It is submitted that a ratio of 1:5.34 does not fall provide the requisite motivation to one of ordinary skill in the art to do what the Inventors of the captioned application have claimed. For this reason, the rejection is improper and should be withdrawn..

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims is respectfully requested. Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Respectfully submitted,

By: _____

Timothy E. Tracy
Reg. No. 39,401

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6586
Dated: August 29, 2003